REMARKS

The Invention.

The present invention provides a novel endoglucanase nucleic acid sequence, designated *egl6*, and the corresponding EGVI amino acid sequence. The invention also provides expression vectors and host cells comprising a nucleic acid sequence encoding EGVI, recombinant EGVI proteins and methods for producing the same.

Status of the Application.

Claims 2, 4-17, 19-20, 22-24 and 26 are pending in the application. Applicants gratefully acknowledge that Claims 23 and 24 are deemed allowable. Applicants reserved the right to file further continuation applications on any subject matter disclosed in the instant application or on the subject matter of any previously or presently cancelled claim. Claims 2, 8, 22 and 26 have been amended to more clearly and distinctly claim the invention. Applicants assert new matter has not been introduced by the amendment.

Specification.

The disclosure was objected to as containing an embedded hyperlink and/or other form of browser-executable code. Applicants have amended the specification to remove the hyperlinks as suggested by the Examiner. Withdrawal of the objection is respectfully requested.

Sequence Compliance.

The Examiner has objected to the introduction of a new SEQ ID NO. and requested its cancellation. Applicants have complied and have rewritten Claim 1 based on the existing sequences.

35 U.S.C. §112, first paragraph.

Claims 2 and 5-7, 10, 12-17 and 19-20

Claims 2 and Claims 5-7,10, 12-17 and 19-20 stand rejected under 35 USC §112, first paragraph as failing to be described in the specification. Specifically, the Examiner asserts that the use of SEQ ID NO:5 constituted "new matter". Applicants have amended Claim 2 to remove reference to SEQ ID NO:5. Withdrawal of the rejection is respectfully requested.

Claims 2, 4-17, 19-20, 22 and 26

Claims 2, 4-17, 19-20, 22 and 26 stand rejected under 35 USC §112, first paragraph as failing to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Specifically, the Examiner assert that the claims are so broad as to encompass any polynucleotide from any source encoding an endoglucanase, vectors, host cells, and method or expressing said endoglucanase and a host cell expressing an inactivated endoglucanase. Applicants respectfully traverse.

It is well settled that "[t]he first paragraph of section 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). Moreover, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 USPQ at 369.

Despite the disclosure of utility in the specification, the Examiner rejected the claims. The reasoning provided in the Office Action was that the genus of DNA molecules encoding the fungal EG VI is "a large variable genus with the potentiality of having many different structures." Applicants respectfully submit that this reasoning is not sufficient to render the claims nonenabled. Applicants respectfully submit that the single species disclosed in the present application is more than sufficient to inform those of skill in the enzyme art that Applicant was in possession of the claimed invention.

The claimed polynucleotides are structurally similar because they hybridize under specified stringency conditions with the nucleic acid sequence of SEQ ID NO: 4 and/or encode an amino acid sequence that is at least 95% identical with the amino acid sequence of SEQ ID NO: 2 or at least 90% identical with the amino acid sequence presented in Figure 2 and the encoded amino acid sequence has endoglucanase

activity. One of ordinary skill in the art therefore would expect that the claimed would not be as variable as the Examiner asserts.

Moreover, companies which develop enzymes are able to produce and screen thousands of enzymes (and the polynucleotides that encode them) in a short period of time. Indeed, enzyme companies have developed automated robotic systems for producing and screening enzymes.

Furthermore, a person skilled in the art can, as a matter of routine, sequence and determine homology of any protein with the EG VI described by Applicants. In addition, Applicants have provided assays at page 32, line 3 *et seq.* to determine enzymatic activity that are also routine in the art.

The Examiner asserts that Applicants have not taught "a single universal method" for isolating polynucleotides or inactivating polynucleotides (see paragraphs bridging pages 8-9 and 10-11 of the Office Action). Applicants respectfully note that "a single universal method" is not required for patentability and Applicants must respectfully disagree with the Examiner's argument and rationale, as the present Specification teaches how to produce variations in the nucleotide sequence (*See e.g.*, page 20 of the Specification), as well as how to determine whether the mutated *egl6* falls within the Claims (*See e.g.*, pages 31 and 37 of the Specification as well as knowledge in the art), and methods for detecting homologues of *egl6* (*See e.g.*, pages 10 and 36 - 38 of the Specification), and methods for determining endoglucanase activity (*See e.g.*, page 32 of the Specification). Applicants respectfully submit that both the structure and function of the endoglucanase encoding polynucleotides claimed are provided in the Specification, as the amino acid sequence (base structure), its glycosyl family classification (See page 24 of the Specification) and function (endoglucanase activity) are well-described throughout the Specification.

The Examiner has stated the Mosimann *et al.* reference submitted previously by the Applicants fails to sufficiently address the issue of unpredictability in the art because it does not explicitly discuss endoglucanase. The Examiner has not provided any reason why a general principle would not be applicable to a specific protein, i.e., an endoglucanase. Applicants fail to understand how a paper directed to proteins generally

fails to be applicable to endoglucanases specifically. The reference addresses numerous proteins (*i.e.*, seven different proteins) of *undisclosed tertiary structure*. In the instant case, the Applicants have provided not only the primary sequence but also the glycosy hydrolase family classification of the endoglucanase. One skilled in the art would recognize that the family classification provides information on the folding characteristics and mechanism of action of these enzymes of the protein (i.e., enzyme). Thus, one skilled in the art would be starting with more information than what was provided in the Mosimann study and would therefore be able to predict at least to the same degree of confidence for an endoglucanase as for the other proteins studied.

The fact that Applicants do not explicitly provide examples regarding every polynucleotide encoding an endoglucanase encompassed by the present claims does not render the present claims unpatentable. Contrary to the Examiner's arguments, Applicants are NOT required to describe in detail each and every embodiment of the presently claimed invention. Indeed, description of a representative number of species does not require that the Applicant describe each and every species. As indicated in MPEP §2163(II)(A)(3)(a)(ii), "[s]atisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., *Eli Lilly*. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces."

In the instant case, the claims are drawn to a specific endoglucanse. The specification need not teach one skilled in the art how to determine whether each embodiment within the scope of the claims is operable. Rather, the specification must teach how to make/or use each embodiment within the scope of the claims <u>without undue experimentation</u>. And, since the specification teaches how to make an endoglucanase (and one skilled in the art using the specification as well as the art

available at the filing date of the application could determine, case by case, whether each additional embodiment, each additional endoglucanase, could be made and was operable), and that it was well known prior to the filing of the instant application that molecular modeling could help predict which alterations in the protein would be tolerated, the specification is sufficient under 35 USC 112, first paragraph for each and every embodiment of the claimed invention. For the foregoing reasons, Applicants submit that the claims overcome this rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 22 and 26

Claims 22 and 26 stand rejected under 35 USC §112, first paragraph as allegedly containing subject which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that the specification does not contain any disclosure of the structure of all DNA sequences that are encompassed by the claims. Applicant respectfully traverses.

Although Applicants respectfully disagree with the Examiner, in order to further the prosecution of the present application and Applicant's business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claims 22 and 26 to recite that the polynucleotide is according to Claim 2.

For the foregoing reasons, Applicants submit that the claims overcome this rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

35 U.S.C. §112, second paragraph.

Claims 8, 9 and 11 are rejected under 35 USC §112, second paragraph as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 9 and 11

Here the Examiner asserts that the phrase "intermediate to high stringency" is not clear and that the phrase "high stringency" should be used. Although Applicants

respectfully disagree with the Examiner, in order to further the prosecution of the present application and Applicant's business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 8 to recite "high stringency". Withdrawal of the rejection is respectfully requested.

35 U.S.C. §102(b).

Claims 8-9 and 11 stand rejected under 35 USC §102(b) as being anticipated by Shin *et al.* Specifically, the Examiner asserts that Shin *et al.* teaches all of the elements of the claims. Applicants respectfully traverse.

Shin *et al.* teaches that their endoglucanase has an ORF of 1254 bases. According to Figure 1 of Shin et al., the gene is cut but *Bam* HI, *Eco* RI and *Xba* I. Applicants provide a restriction map of their gene and note that the restriction map is not similar. The genes simply are not the same.

Withdrawal of the rejection is respectfully requested.

35 U.S.C. §103.

The Examiner has maintained the rejection of Claim 26 as allegedly obvious over the combination of Shin, *et al.* in view of Ward, *et al.* (US Pat. No. 6,265,204; the '204 patent). Applicants respectfully traverse the rejection.

The Examiner asserts that those skilled in the art would have been motivated to use the polynucleotide sequence provided by Shin *et al.* (applicants respectfully note that no DNA sequence was provided by Shin *et al.*) and introduce it into vectors provided by Ward et al. and express the same in a filamentous fungal host cell such as *Aspergillus*. Applicants disagree.

First, as the skilled artisan readily recognizes, yeast are excellent hosts for heterologous protein production, since they can be grown to high cell densities on simple media and many proteins can be correctly folded and secreted to the culture medium. The advantages of using *S. cerevisiae* as host for production of proteins are numerous, including ease of genetic manipulation, ability of performing post-translational modifications, ease of growth and well established industrial processes.

Second, the Examiner asserts that the motivation to combine the two because "Ward et al. teach that filamentous fungus host cells secrete the polypeptide into the culture medium" (see page 16 of the Office Action). However, as noted in the abstract of Shin et al., "[i]rrespective of host strain, about 80% of the expressed endoglucanase was detected in the extracellular medium." Thus, the skilled artisan already had a host cell that secreted the endoglucanase.

Finally, if Shin *et al.* were adding the cellulolytic enzyme to the yeast in order to provide an organism that could degrade cellulose to fermentable sugars then there would be no motivation to move to another host that was capable of producing cellulolytic enzymes but not able to ferment the sugars. This may be what they were trying to achieve as there is reference to "cellulolytic yeast" in the first paragraph.

Thus, for the reasons given above, Applicants believe that the skilled artisan would not have been motivated to move to another host organism. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In light of the above amendments, as well as the remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7615.

Respectfully submitted,
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